REMARKS

Claims 1, 4-26 and 35-38 are pending. Claims 1, 4, 7 and 8 were examined and are rejected by the Examiner in the final Office Action. Applicants respond below to the specific rejections raised by the Examiner. For the reasons set forth below, Applicants respectfully traverse.

Rejection Under 35 U.S.C. § 103(a)

Claims 1, 2, and 4

The Examiner has rejected Claims 1, and 4 under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Ho et al. (2002) *Angew. Chem. Int.* 41:1548-1551 in view of Gold (1995) *JBC* 270:13581-13584, for the reasons set forth in the Office Action mailed October 7, 2008. Specifically, the Examiner maintains that Ho et al. teach an optical sensor comprising a ssDNA complementary to a target and the same, water-soluble, cationic polythiophene derivative of the formula shown in Claim 1. The Examiner concedes that Ho et al. do not specifically teach that the ssDNA of the optical sensor is an aptamer. However, the Examiner states that Gold teaches that aptamers are single-stranded DNA molecules that interact with target molecules and that aptamers are useful for detecting proteins. According to the Examiner, it would have been obvious for one skilled in the art to substitute the ssDNA in the polythiophene-ssDNA complex disclosed by Ho et al. by an ssDNA aptamer taught by Gold for the purpose of detecting target molecules.

In determining whether a case is obvious under 35 U.S.C. § 103(a), the references and teachings must be viewed as a person of skill in the art would view the references. (See, M.P.E.P. §2141). Further, the art must be such that the skilled artisan would have a reasonable expectation of success at practicing the claimed invention. As explained below, the Office Action mailed October 7, 2008 fails to establish that Claims 1 and 4 are *prima facie* obvious over Ho et al. and Gold since the references would not provide the skilled artisan with any expectation of successfully modifying the cited references to arrive at Applicants' presently claimed invention.

Ho et al. teach that polythiophene derivatives can be used to detect specific single-stranded oligonucleotides by using a polythiopchene derivative and a "capture probe" that is a single stranded oligonucleotide that is substantially complementary to the target ssDNA In

particular, Ho et al. teach the use of water-soluble polythiophene derivatives to "transduce **oligonucleotide hybridization with a specific 20-mer capture probe** into a clear optical (colorimetric or fluorometric) output." *See* Ho et al. p.1549, first column (emphasis added). According to Ho et al., the underlying principle behind the usefulness of polythiophene derivatives as reagents to detect hybridization events is that the electrostatic interactions and conformational structures formed when the polythiophene derivatives are in contact with the single-stranded oligonucleotides (the "capture probe") differ from the electrostatic interactions and conformational structures formed when the polythiophene derivatives are in contact with double-stranded (hybridized) nucleic acids, *i.e.*, in the presence of a target hybridizes to the capture probe.

According to Ho et al., when the polythiophene derivatives are contacted with a ssDNA capture probe, a polythiophene/ssDNA "duplex" is formed, which has a characteristic UV absorption spectra. When the polythiophene derivatives are contacted with a ssDNA capture probe that hybridizes to a ssDNA target, a polythiophene/dsDNA "triplex" is formed, which has different absorbance (and fluorescent) properties. In other words, the teachings of Ho et al. teach that the hybridization of the capture probe and target to form a dsDNA is essential for the detection via the polythiophene derivative. Accordingly, at most, one skilled in the art would conclude from Ho et al. that the polythiophene derivatives could be used to detect ssDNA targets that hybridize to the capture probe/aptamer.

As stated in Applicants' previous response, Claim 1 is drawn to optical sensors for the detection of potassium ions, small organic molecules, amino acids, proteins, whole cells and nucleotides. None of the "targets" recited in Applicants' claims form dsDNA in the presence of a ssDNA aptamer. As such, they would not form a polythiophene/hybridized nucleic acid triplex, and the skilled artisan would have no reason to expect that their presence could be detected by an optical sensor comprising a polythiophene derivative and a ssDNA aptamer, given the teachings of Ho et al., which merely teaches that the optical properties of polythiophene derivatives change in the presence of ssDNA versus dsDNA. Accordingly, one skilled in the art would not have had a reasonable expectation of success in using the polythiophene derivatives for the purpose to detect the targets recited in amended Claim 1.

In response to Applicants' arguments, the Examiner states that the rejection is maintained because "'nucleotides' are recited as a target in claim 1, and the detected oligonucleotides in the Ho reference are comprised of oligonucleotides." (Office Action, at 3). Applicants respectfully submit that the Examiner has overlooked the fact that the basis of the use of polythiophenes in Ho et al. depends upon the hybridization between a single stranded oligonucleotide "aptamer" and its complementary target. Although the PTO has taken the position that oligonucleotides "are comprised of nucleotides," this does not establish obviousness. More accurately, oligonucleotides are polymers formed from nucleotide monomers. That formation involves a chemical reaction in which some atoms of the original nucleotide are split off and new covalent bonds are formed to generate a new chemical entity. Nucleotides (which are monomers) and oligonucleotides (which are polymers) have very different properties. The property relied upon by Ho et al. is specific hybridization, a property that is unique to the polymer. This in turn forms double stranded duplexes that Ho et al. explain can be detected in the presence of polythiophene derivatives. Nucleotides themselves, as recited in Applicants' claims, are distinct chemical entities that will not "hybridize" and form "dsDNA" in the presence of target DNA. Thus, the "triplexes," *i.e.*, dsDNA complexed with the polythiophene derivative, would not be formed in the presence of "nucleotides." Accordingly, one skilled in the art would not have a reasonable expectation of success, given the teachings of Ho et al.

As stated by the Examiner, the Gold reference is relied upon merely for the teaching that aptamers are ssDNA molecules that can bind specific target molecules. Gold is completely silent about polythiophene derivatives. Thus, Gold does not provide the skilled artisan with any reason to expect that polythiophene derivatives can be used in any way.

In view of the foregoing, Applicants respectfully submit that the teachings of Ho et al. and Gold do not provide the skilled artisan with any reason to expect that polythiophene derivatives can be used in optical sensor to detect targets such as potassium ions, small organic molecules, amino acids, proteins, whole cells and nucleotides. As such, the references cannot support a *prima facie* case of obviousness under 35 U.S.C. § 103(a). Applicants respectfully request reconsideration and withdrawal of the rejection accordingly.

Finally, the Examiner's withdrawal of the rejection of Claims 7 and 8, (which ultimately depend from Claim 1), under 35 U.S.C. § 103(a) over Ho et al., Gold and Michaud et al. (2004)

Analytical Chemistry 74:1015-20, would appear to indicate that the Examiner agrees that Claims 1 and 4 are patentable over Ho et al. and Gold. Specifically, Michaud et al. was relied upon solely for the teaching of D-adenosine-specific aptamer having the exact sequence of SEQ ID NO:3. Accordingly, there is no teaching in Michaud et al., that would appear to add to the teachings of Ho et al. and Gold, to render Claims 1 and 4 obvious. For this further reason, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 1, 4, 7 and 8

The Examiner has rejected Claims 1, 4, 7 and 8 under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Michaud et al., Ho et al., McQuade et al. (2000) *Chem. Rev.* 100:2537-3574, Gold, and Nilsson (2002) *J. Phys. Condens. Matter* 14:10011-10020. The Examiner asserts that Ho et al. teach an optical sensor comprising an oligonucleotide that is complementary to a ssDNA target, and that "optical sensors could be used for the detection of DNA-hybridization events." (Office Action, at 4). The Examiner concedes that Ho et al. do not teach that the oligonucleotide is an aptamer, but argues that Michaud et al. teach that the oligonucleotide of SEQ ID NO:3 is an adenosine-specific aptamer, and that Gold teaches that aptamers can be modified with "visualization-enhancing adducts or reporters," (Id.), to be used for "detecting proteins." (Id.). The Examiner argues that McQuade et al. teach that "polythiophene antibody complexes are effective biosensors" (Id. at 5), and that Nilsson et al. teach that conjugated polythiophenes can be used to couple analyte-receptor interactions. The Examiner also states that Nilsson et al. teach and that conjugated polythiophenes are very sensitive to very minor perturbations. As such, the Examiner argues that one skilled in the art would recognize that the use of polythiophene in an aptamer-based sensor would function.

Applicants respectfully traverse, and submit that the teachings of the cited references, alone or in combination, would not provide the skilled artisan with the requisite reasonable expectation of success to support a *prima facie* case of obviousness. As set forth above, Ho et al. merely suggest that the polythiophene derivatives recited in Claim 1 can be used to detect oligonucleotide/ssDNA hybridization events, and that this occurs through the formation of a "triplex" between the hybridized nucleic acid molecules and the polythiophene derivative. There is nothing in Ho et al. that would lead the skilled artisan to reasonably expect that an "aptamer-

target" could be substituted for the "oligonucleotide/ssDNA target" described in Ho et al., and that such a compound could be used to detect a target as recited in Applicants' claims.

The Examiner relies upon the teachings of McQuade et al and Nilsson et al. as allegedly providing teachings that would lead the skilled artisan to reasonably expect that the aptamer/target could be substituted for the oligonucleotide/complementary target of Ho et al. Applicants respectfully submit, however, that the Examiner's assertion that Figure 24, p. 2567 of McQuade et al. shows that "polythiophene-antibody complexes are effective biosensors," is misplaced, and, further, that the teachings of McQuade et al. do not establish that one could effectively use Applicants' claimed compositions as optical sensors.

As an initial matter, McQuade et al. are completely silent regarding the specific polythiophene derivatives required in Applicants' claims. Furthermore, the alleged "biosensor" depicted in Figure 24 of McQuade et al. is completely different from Applicants' claimed optical sensor. Figure 24 depicts a polythiophene conjugated to a platinum surface. (McQuade, p. 2567, Col. 2, 2nd paragraph). The polythiophene-coated platinum surface is contacted with magnetic beads functionalized with antibodies specific for atrizine, in the presence or absence of atrizine or atrizine-glucose kinase. After contact with atrizine, the capacitance current is measured. (McQuade, p. 2568m Col 1, 1st paragraph.) The polythiophene shown in Figure 24 is not a "polythiophene-antibody sensor" as suggested by the Examiner. In fact, the polythiophene shown in Figure 24 of McQuade et al. is not even an "optical sensor," as there is no mention of optical measurement in connection with Figure 24.

Elsewhere on page 2567, McQuade et al. describe "antigens" labeled with polythiophene derivatives of unspecified structure. McQuade et al. report that upon binding a corresponding antibody, the optical density of the polymer band at 380 nm was observed to increase with increasing concentration of cognate antibody. McQuade suggests that the increase in polymer absorbance is due to "local pH change[s] that occur[] when the antigen and antibody bind." (McQuade, 2567, Col. 2). McQuade is completely silent about the use of an optical sensor that includes an oligonucleotide that binds to an aptamer. There is no scientific basis that would lead the skilled artisan to assume that an antigen/antibody interaction could and would provide the same type of environment as an oligonucleotide/aptamer interactions, or that the association between the polythiophene derivative and a protein, and the polythiophene derivative and an

oligonucleotide, would be similar. As such, there is no scientific basis for the assertion that the skilled artisan, in view of the teachings of McQuade et al., would have a reasonable expectation of successfully arriving at Applicants' claimed optical sensors.

According to the Examiner, Nilsson et al. teach that "polythiophenes [in general] are sensitive to minor perturbations." The Examiner relies upon this single statement, as evidence that would suggest that Applicants' claimed optical sensors would work. As with McQuade et al., however, Nilsson is completely silent about the particular optical sensors recited in Applicants' claims. In fact, Nilsson et al. relates to "amino-acid-fucntionalized polythiophene[s]." (Nilsson et al., Title). Further, as with McQuade et al, Nilsson et al. provide no teaching that would lead the skilled artisan to reason that polythiophenes, and, in particular, Applicants' presently claimed polythiophenes, can be combined with single stranded oligonucleotide aptamers, to detect targets. Accordingly, Nilsson et al. does not cure the deficiencies of the other cited references, in establishing a *prima facie* case of obviousness.

In view of the foregoing, Applicants respectfully submit that Michaud et al., Ho et al., McQuade et al., Gold, and Nilsson et al. fail to provide the skilled artisan with a reasonable expectation of success, and therefore do not support a *prima facie* case of obviousness under 35 U.S.C. § 103(a). Applicants respectfully request reconsideration and withdrawal of the rejection accordingly.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

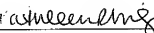
In view of the above amendments and remarks, Applicants respectfully maintain that the claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: September 18, 2009

By: 

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